REMARKS

Upon entry of the present amendment, claims 1-36 will be pending. Claims 1-10 and 17-36 stand withdrawn (as Applicants wish to retain their right to rejoinder), and claims 11-16 are under examination. Claim 11 has been amended to improve its clarity; claim 12 has been amended to change the term "cell" to "cells"; and each of claims 13-16 have been amended to perfect the reference to an antecedent term. No new matter has been added.

Information Disclosure Statement

Applicants thank Examiner Kosar for the explanation regarding the Information Disclosure Statement. A further Information Disclosure Statement may be filed to explain the relevance of the references for which an incomplete English language version was previously submitted.

Claim Objections

The Examiner objected to claim 12 because "the phrase 'the number of the hair dermal papilla cell" appears to be a typographical error of the phrase 'the number of hair dermal papilla cells'" (Office action at page 3; emphasis in original). Applicants thank the Examiner for pointing out this error, which has been corrected by way of the present amendment.

35 U.S.C. 101

The Examiner has rejected claims 11-16, alleging that "the claimed invention is not supported by either a specific and substantial asserted utility or a well-established utility" (Office Action at page 3). After referring to the MPEP at § 2107.01(I), the Examiner further argues that, although "[t]he instant claims are asserted to be hair follicle-regenerating compositions," Chuong *et al.* (*J. Invest. Dermatol.* 127:2098-2100, 2007) characterizes a study related to the composition presently claimed as "work in progress" toward the goal of engineering a "real" human hair follicle (Office action at pages 4-5).

In view of the present amendment and the remarks that follow, the Examiner is asked to reconsider and withdraw this ground for rejection. Both the MPEP at § 2107.01 and the case law strongly support a finding of utility in the present case. Generally, there are two situations in which utility is truly lacking, and neither of those apply here.

In the first, it is not apparent why the invention is useful. MPEP at § 2107.01, citing *Brenner v. Manson*, 383 U.S. 519, 148; *In re Fisher*, 421 F.3d 1365, 76 (Fed. Cir. 2005); and *In re Ziegler*, 992 F.2d 1197 (Fed. Cir. 1993). Preparations that can be used to repair various injuries to the skin or to improve the skin's appearance are clearly useful. A great deal of research has been carried out in this field, and the present specification refers repeatedly to donor tissues, transplantation, and skin equivalents. The repair of the skin, due to injury or other deficiencies (such as unwanted hair loss) constitutes a specific and substantial utility.

"The second type of deficiency arises in the *rare instance* where an assertion of specific and substantial utility ... made by an applicant is not credible." (MPEP at § 2107.01; emphasis added). As reviewed in the MPEP, and with respect to credibility, "the Federal Circuit has stated, '[t]o violate [35 U.S.C.] 101 the claimed device must be totally incapable of achieving a useful result.'" MPEP at § 2107.01 citing *Brooktree Corp. v. Advanced Micro Devices, Inc.*, 977 F.2d 1555, 1571, (Fed. Cir. 1992) (emphasis added). Further, in *E.I. du Pont De Nemours and Co. v. Berkley and Co.*, 620 F.2d 1247, 1260 n.17, 205 USPQ 1, 10 n.17 (8th Cir. 1980), the court stated:

> A small degree of utility is sufficient . . . The claimed invention must only be capable of performing some beneficial function . . . An invention does not lack utility merely because the particular embodiment disclosed in the patent lacks perfection or performs crudely . . . A commercially successful product is not required . . . Nor is it essential that the invention accomplish all its intended functions . . . or operate under all conditions . . . partial success being sufficient to demonstrate patentable utility . . . In short, the defense of non-utility cannot be sustained without proof of total incapacity.

Thus, it is not necessary for the present inventors to have produced a dermal papilla cell preparation that functions perfectly. That is not the standard for a credible utility. Technology necessarily evolves; patents are not granted only for the ultimate inventions. The present

inventors' discovery of methods that can be used to make a dermal papilla cell preparation represent an improvement over prior methods. A specific and substantial use has been asserted, and that use is credible according to the prevailing legal standard. Accordingly, this ground for rejection should be withdrawn.

35 U.S.C. § 112, first paragraph

With respect to enablement, the Examiner argues that, since the claimed invention has no utility, "to the extent the claims are drawn to a follicle-regenerating composition one skilled in the art clearly would not know how to use the claimed invention" (Office action at page 5; emphasis in original). The Examiner then goes on to analyze claims 11-16 in accordance with *In re Wands* (858 F.2d 731 (Fed. Cir. 1988)), which established that, experimentation is permitted in order to make and use an invention so long as that experimentation is not "undue." In view of the present amendment and the remarks that follow, the Examiner is asked to reconsider and withdraw this ground for rejection.

As set out in the specification (*see, e.g.*, the paragraph bridging pages 3-4), the compositions now claimed are based on Applicants' discovery that subjecting a dermal tissue, which includes both hair dermal papilla cells and follicular epidermal cells, to extremely low temperatures (such as those used for cryopreservation), causes the epidermal cells to die but allows the dermal papilla cells to survive. Based on this discovery, it became possible to obtain, from a sample of skin, a cell preparation comprising hair dermal papilla cells as the active cellular component. By combining such a preparation with a preparation that includes only epidermal cells, it was then possible to determine the ratios of the two cell types (as is set out in claim 11) that gave rise to useful compositions for skin repair and/or hair growth (even if not completely equivalent to natural hair growth in all cases).

Independent claim 11 covers a composition made by a particular method, the steps of which reflect the discoveries described above. One must provide skin tissue; remove epidermal tissue from the skin tissue, thereby producing a dermal tissue fraction; subject the dermal tissue fraction to collagenase treatment, thereby producing a cell suspension comprising hair dermal

papilla cells; cryopreserve the cell suspension to kill the follicular epidermal cells present in the cell suspension, thereby producing a hair dermal papilla cell preparation; and mix the preparation with active epidermal cells so that the ratio of the number of hair dermal papilla cells to the number of epidermal cells is from 1:10 to 10:1. Applicants specification clearly describes how to make and use compositions made by carrying out these steps, and there is no reason why one of ordinary skill in the art could not do the same. Claim 11 does not require compositions capable of perfect hair follicle regeneration; the compositions claimed meet the utility requirement; there is a strong correlation between the teaching provided by the specification (which is discussed further below) and the breadth of the claim; and claims may cover some inoperative embodiments (*Atlas Powder Co. v. E.I. du Pont de Nemours & Co.*, 750 F.2d 1569, 224 USPQ 409 (Fed. Cir. 1984)). For these reasons alone, the rejection for enablement should be withdrawn.

The Office alleges that two references, which have not yet been discussed, Inamatsu *et al.* (U.S. 5,851,831; "Inamatsu") and Stenn *et al.* (*J. Invest. Dermatol.* 128:1576-1578, 2008; "Stenn"), establish that "follicle regeneration is unresolved" (Office action at page 7). Applicants respectfully disagree. Inamatsu describes methods of culturing dermal papilla cells, but does not teach methods of purifying dermal papilla cells by placing them at a cryopreserving temperature. Stenn reviews the hypothesis that hair follicles co-evolved with sebaceous glands, but is completely silent as to methods of purifying dermal papilla cells. Thus, these references, while in the field of the invention, do nothing to establish that compositions *made by the steps required by the present claims* are unpredictable.

The amount of guidance provided by the specification and the level of skill in the art also weigh in favor of enablement. For example, the specification at page 7, line 8, to page 8, line 14 provides guidance on how to purify dermal papilla cells from mammalian tissue (by cryopreservation), and also how to quantify these cells. The specification teaches that dermal papilla cells may be isolated from any one of the numerous mammals (specification at page 8, lines 15-23). The specification provides guidance on how to prepare epidermal cells, for example, at page 9, lines 1-17 and teaches that epidermal cells may be prepared from any one of

the mammals that were also listed for purification of dermal papilla cells (specification at page 9, lines 18-27). The specification teaches that dermal papilla cells and epidermal cells can be mixed at different ratios, including the ratios required by the present claims, and transplanted into a recipient animal (specification page 9, line 28, to page 10, line 12). Further, there are a number of working examples. In view of the foregoing, this ground for rejection should now be withdrawn.

35 U.S.C. § 112, second paragraph

The Examiner alleges (at pages 10-14 of the Office Action) that claims 11-16 are indefinite for various reasons.

The Examiner states that "[t]he claims are indefinite, because, the recitations and correlations of the terms 'epidermis', 'epidermal cells', 'epidermal tissue', and 'follicular epidermal cells' in claim 11 are unclear" (Office Action at page 10).

As a first point, claim 11 does not recite "epidermis." As a second point, Applicants have amended claim 11 to more clearly distinguish between the "follicular epidermal cells" that are killed to obtain the dermal papilla cell preparation and the "active epidermal cells" that are mixed with the dermal papilla cell preparation to produce the composition. Claim 11 has also been amended to make it clear that the "epidermal tissue" is removed from skin tissue to produce a dermal tissue fraction from which the dermal papilla cell preparation is prepared.

The Examiner further noted that method steps should "minimally include a *contacting/reacting step* in which the reagents and reactions of the reagents are recited and a *correlation/concluding step* describing the results of the reaction" (Office action at page 11; emphasis in original). Claim 11 has been amended to address this concern, as it now requires "mixing the preparation with active epidermal cells" (which is a contacting/reacting step) "thereby producing the composition" (which is a correlation/concluding step).

Two terms were discussed with respect to antecedent basis: "the cell suspension" and "the follicular epidermal cells" (Office action at page 12). In response, claim 11 has been amended to refer first to "*a* cell suspension" and thereafter to "*the* cell suspension." Claim 11

has also been amended to specify that the follicular epidermal cells are "present in the cell suspension" and, for that reason, Applicants contend that the term is clear.

Claim 12 was rejected due to inclusion of the term "about" (Office action at page 13). Applicants respectfully disagree. One of ordinary skill would understand that the term "about 1:1" indicates that the ratio of dermal papilla cells to epidermal cells need not be exactly 1:1, which would be impractical, if not impossible, to determine. Further, the doctrine of claim differentiation holds that two claims in the same patent will not have the same scope. Claim 12, which recites "about 1:1" depends from claim 11, which recites the broader range of "from 1:10 to 10:1." Thus, the most reasonable interpretation is that "about 1:1" further limits "from 1:10 to 10:1".

Finally, in response to the Examiner's concern regarding the units of measure, claim 13 has been amended to recite "adjusting the cell density of the cell suspension to 1×10^5 to 1×10^8 cells/ml" (emphasis added).

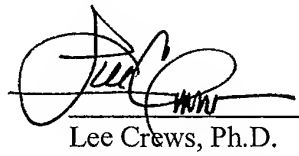
If the Office is implying that in order to be definite, the claims need recite (a) the temperature at which the density measure is taken and (b) the density of the solvent, Applicants respectfully disagree. Claim 13 makes clear that "cryopreserving the cell suspension is carried out after adjusting the cell density of the cell suspension from 1×10^5 to 1×10^8 cells/ml". The temperature at which the cell density measurement is taken (or the solvent in which the cells are suspended) is irrelevant since given any particular temperature (or solvent), one of ordinary skill could adjust the cell density according to claim 13.

In consideration of the amendments and comments provided above, Applicants respectfully request that the claim rejections for indefiniteness on this ground be withdrawn.

The Petition for Extension of Time fee is being paid concurrently on the Electronic Filing System (EFS) by way of Deposit Account authorization. Please apply any other charges or credits to deposit account 06-1050, referencing Attorney Docket No. 23757-009US1.

Respectfully submitted,

Date: July 9, 2008



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